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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,219	12/12/2001	Hiroharu Matsuoka	MATSUOKA=18	7465

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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
02/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/890,219	MATSUOKA ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Remarks/Declaration filed 10/19/07*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,13-25,28-30 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,13-25,28-30 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The 112, first paragraph rejection of the term "hydrates" in claims 1-9, 13-25, 28-30, and 35 made in the office action filed 6/20/07, is rendered moot in light of applicant's amendments filed 10/19/07. The 102 (b) rejection over Hcaplus 101:66177 is rendered moot in light of applicant's amendment filed 10/19/07.

(modified Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 13-25, 28-30, 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds of formula I wherein R12 is OH, R13 is T-Bu, OH, R9 is isopropyl, or –CH2CF3, R7 is NH2, R10 is H, Et, Me, X is Carbonyl, R8 is methyl, R11 is amide, C(O)NHMe, C(O)NHEt, C(O)NHCH2OH, C(O)NHCH2SO2CH3, C(O)NHCPr, CO)CPr, CO)nPr, C(O)Pr, R7 is alkyl substituted amino, R10 is H, Me, Et, n-propyl, and its intermediate of formula 6 with the corresponding moieties, does not reasonably provide enablement for using the compounds with R12, R13, R9, R7, R10, R8, R11 equal to moieties claimed other than those enabled above. The specification does not enable any skilled pharmacologist or physician to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above.

a) Determining if any particular claimed compounds with R12, R13, R9, R11, R7, R10 equal to the moieties other than those enabled above, would be active would require synthesis of the substrate and subjecting it to testing with Applicants' Motilin receptor binding assay and contraction suppressing test. Considering the large number of compounds to be made this is a large quantity of experimentation. b) The direction concerning the claimed compounds is found in pages 35-41, 44-60, which merely states Applicants' intent to make and use such compounds. c) In the instant case none of the working examples contains any R12, R13, R9, R11, R7, R10 equal to the moieties other than those enabled above. d) The nature of the invention is antagonizing of the motilin receptor and treatment of human diseases with Applicants' compounds. This involves physiological activity. The nature of the invention requires an understanding of the motilin receptor, the binding activity of small ligands to that receptor, and the ability of those compounds to antagonize that receptor. In view of the unpredictability of receptor binding activity and claimed divergent substituents with varied polarity, size, and polarisability, the skilled physician would indeed question the inclusion of compounds with such diverse moieties, commensurate in scope with these claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

e) There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (I) will all share the same biological properties. The diverse claimed compounds are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally

dissimilar compounds will have such activity, *In re Surrey* 151 USPQ 724 (compounds actually tested which demonstrated the asserted psychomotor stimulatory and anti-convulsant properties were those having the 3,4-dichlorophenyl substituent at the 2-position on the thiazolidone nucleus not sufficient for enablement of any heterocyclic radical at the same position). *In re Fouche*, 169 USPQ 429 at 434 (a Markush group including both aliphatic and heterocyclic members not enabled for the use of those compounds within the claim having heterocyclic moieties.) *In re CAVALLITO AND GRAY*, 127 USPQ 202 (claims covering several hundred thousand possible compounds, of which only thirty are specifically identified in appellants' application, not enabled unless all of the thirty specific compounds disclosed had equal hypotensive potency because that fact would strongly indicate that the potency was derived solely from the basic structural formula common to all of them. A wide variation in such potency would suggest that it was due in part to the added substituents and might be eliminated or even reversed by many of the possible substituents which had not been tried.)

f) The artisan using Applicants' invention to treat diseases with the claimed compounds would be a physician with a MD degree and several years of experience. He would be unaware of how to predict *a priori* how a changing a heterocyclic ring would affect biological activity. g) Physiological activity, is well-known to be unpredictable, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510,

1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of millions of compounds of formula (I). Thus, the scope is very broad. The present claims embrace various diverse compounds, which are not art-recognized as equivalent. The specific compounds made are not adequately representative of the compounds embraced by the extensive Markush groups instantly claimed.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

(new rejection)

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-25, 28-34, 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-7, 10-14 of U.S. Patent No. 6225285. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent teaches a genus of compounds and compositions which overlap in subject matter with the instant genus of compounds and compositions.

'285 teaches the genus of compounds of formula I, and the composition containing them, wherein A is an amino acid residue, provided that A binds with -NR2- to form an amide, R1 is an optionally substituted straight-chained or ranched alkyl group having 2-7 carbon atoms, R2 is a hydroen atom or an optionally substituted straight-chained or branched alkyl group having 1-3 carbon atoms, R3 is –COR7, R5 is –OR8, RR7 is –N(R12)R13, R8 is a hydrogen atom or a straight-chained alkyl group having 1-4 carbon atoms, R12 and R13 which may be the same or different represent a hydrogen atom, a straight-chained or branched alkyl group having 1-4 carbon atoms. At columns 90 and at column 91, lines 1-35, see the compounds defined. The difference between the prior art compound and compositions and the instantly claimed compounds and compositions is a teaching of a generic compound and composition which overlaps in subject matter with the instant genus and compositions. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare

structurally similar compounds and compositions. Accordingly, the compounds and compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds and compositions over those of the generic prior art compounds and compositions.

(Response to Applicant's Arguments)

The Obvious Double Patenting Rejection was instituted over Kotake because of the obvious subject matter. This Kotake reference was used as a 103 (a) in the office action dated 6/20/05. Applicant did not dispute the obviousness of this reference, but stated that this reference was published after the filing date. However, since a filing date does not pertain to an obvious double patenting rejection with regard to a patent, and the Kotake Reference is a patent which shares a common inventor, an obvious double patenting rejection is required.

The declaration filed 10/19/07 is insufficient to overcome the 112, first paragraph rejection above because the evidence submitted is not commensurate in scope with the claims, but is basically the same scope of the compounds stated to have been enabled in the last outstanding office action filed 6/20/07. This scope does not enable the full scope of the compounds because the present claims embrace various diverse compounds outside of this scope, which are not art-recognized as equivalent. For example, R7 equal to NH2 is not recognized as art equivalent to R7 equal to hydroxy; R14 equal to piperidine is not art recognized as R14 equal to an oxane. The specific compounds made are not adequately representative of the compounds

embraced by the extensive Markush groups instantly claimed. Therefore, the 112, first paragraph rejection is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Janet Andres can be reached on 571-272-0867.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

Binta Robinson

BMR
January 31, 2008

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER